



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/358,141	07/20/1999	JEFFREY R. SAMPSON	10990393-1	1170

22878 7590 04/24/2006

AGILENT TECHNOLOGIES, INC.  
INTELLECTUAL PROPERTY ADMINISTRATION, LEGAL DEPT.  
P.O. BOX 7599  
M/S DL429  
LOVELAND, CO 80537-0599

EXAMINER

ZARA, JANE J

ART UNIT	PAPER NUMBER
----------	--------------

1635

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.



UNITED STATES PATENT AND TRADEMARK OFFICE

---

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

**MAILED**  
**APR 24 2006**  
**GROUP 1600**

**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Application Number: 09/358,141  
Filing Date: July 20, 1999  
Appellant(s): SAMPSON, JEFFREY R.

---

Cynthia J. Lee  
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 2-8-06 appealing from the Office action mailed 6-13-05.

**(1) Real Party in Interest**

A statement identifying by name the real party in interest is contained in the brief.

**(2) Related Appeals and Interferences**

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

Application 09/632,639, Examiner's Answer was filed 7-25-05 in response to the Appeal Brief filed 5-9-05.

**(3) Status of Claims**

The statement of the status of claims contained in the brief is correct.

**(4) Status of Amendments After Final**

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5) Summary of Claimed Subject Matter**

The summary of claimed subject matter contained in the brief is correct.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

**(7) Claims Appendix**

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(8) Evidence Relied Upon**

**Exhibit A, page 1 of 1, filed 8-15-05**

<b>6,569,630</b>	<b>Vivekananda et al.</b>	<b>6-1999</b>
<b>5,912,340</b>	<b>Kutyavin et al.</b>	<b>5-2003</b>

**(9) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 25-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Vivekananda et al. for the reasons of record set forth in the Office action mailed 12-22-05 and reiterated below.

Vivekananda et al. (*hereinafter* "Vivekananda") teach methods comprising synthesizing nucleic acid molecules with a reduction or alteration in secondary structure. Vivekananda teaches the synthesis of nucleic acid ligands that contain

modified nucleotides that render intra-strand, complementary nucleotides with a reduced ability to form stable hydrogen bonded base pairs. Vivekananda specifically discloses the incorporation of 2'-amino purines, 2'-thio substituted bases including 2'-thiocytidine and 2'-thiouridine, as well as the incorporation of inosine into nucleic acid ligands through various methods including PCR, RT-PCR, LCR, and several other nucleic acid amplification procedures. Vivekananda teaches the instantly claimed methods of synthesizing nucleic acid polynucleotides with reduced secondary structure by incorporating the claimed modified bases, producing nucleic acid strands with a reduced ability to form intra-molecular base pairs (see especially col. 2, lines 20-65; col. 3, line 44-col. 5, line 67; col. 6, line 62-col. 10, line 31), comprising the polymerization of nucleotide precursors from a DNA or RNA template by an appropriate polymerase or transcriptase (see especially col. 22, line 29-col. 24, line 45), and which nucleotide precursors include 2-aminodeoxyadenosine 5'-triphosphate, 2-thiodeoxythymidine 5'-triphosphate, and inosine triphosphate (see especially col. 20, line 14-col. 22, line 9), whereby a nucleic acid molecule with reduced levels of cross-hybridization is synthesized.

Claims 1 and 25-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Kutyaivin et al. for the reasons of record set forth in the Office action mailed 12-22-05 and reiterated below.

Kutyaivin et al. (*hereinafter* "Kutyaivin") teach methods of synthesizing nucleic acid molecules with reduced or secondary structure (see the abstract; col. 2, line 33-

col. 9, line 53; claims 1-20, 23-25), comprising the polymerization of nucleotide precursors from a DNA or RNA template by an appropriate polymerase or transcriptase, (see col. 18 and 22-23), and which nucleotide precursors include 2-aminodeoxyadenosine 5'-triphosphate, 2-thiodeoxythymidine or -cytidine, 5'-triphosphate, pyrrolo-pyrimidine triphosphate, inosine triphosphate (see col. 5, col. 34, lines 53- 67), whereby a nucleic acid molecule with reduced levels of cross-hybridization is synthesized (see abstract; text in col. 4; claims 1-20). Kuyativin discloses methods of synthesizing polynucleotides with a reduced ability to form self-annealing double strands by incorporating the modified bases claimed, which in turn render polynucleotides with reduced ability to form stable hydrogen bonded base pairs with either a complementary strand or with complementary bases within the same strand (see e.g. col. 1 of Kutyavin: "[t]he ODNs include modified bases of such nature that the modified base forms stable hydrogen bonded base pairs with the natural partner base, but does not form stable hydrogen bonded base pairs with its modified partner... The ODNs of the invention, however, form substantially stable hybrids with the target sequence in each strand of duplex nucleic acid."). The procedure disclosed by Kutyavin, therefore, is indistinguishable from the instantly claimed methods because both methods involve the synthesis of oligonucleotides in the presence of modified bases, to produce nucleic acids with reduced ability to hybridize to complementary bases by reducing the ability to form Watson-Crick base pairing. The characteristic of reduced ability to hybridize to complementary, modified bases exists in intra-molecular as well as inter-molecular complementary nucleic acid strands. The distinction between

inter-molecular and intra-molecular base complementarity is addressed by Kuttyavin within the context of the target sequence: "It is known that secondary structure of mRNA and ribosomal RNA do not have two strands in the strict sense of that term. Nevertheless, unless the context otherwise indicates, in the present description the terminology "two strands" of double stranded nucleic acids also refers to the two complementary portions of duplex mRNA or of duplex ribosomal RNA as well. The general concept of double stranded DNA and of secondary structure ... is covered in this description by the term "duplex nucleic acid." (see col. 4).

#### **(10) Response to Argument**

Claims 1 and 25-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Vivekananda.

Appellant's arguments filed 2-8-06 have been fully considered but they are not persuasive. Appellant argues that Vivekananda does not properly anticipate the claimed invention because Vivekananda does not teach methods of synthesizing nucleic acid molecules with reduced secondary structure, but instead describes their nucleic acids as aptamers, and utilizes nucleic acid molecules that are able to specifically bind particular targets including through non-Watson-Crick interactions.

Contrary to Appellant's assertions, Vivekananda teaches methods of synthesizing nucleic acid molecules with a reduced or altered secondary structure (see especially col. 2, lines 20-65; col. 3, line 44-col. 5, line 67; col. 6, line 62-col. 10, line 31). Vivekananda teaches the polymerization of nucleotide precursors, including 2-

amino deoxyadenosine 5'-triphosphate, 2-thio deoxythymidine 5'-triphosphate, and inosine triphosphate, from a DNA or RNA template by an appropriate polymerase or transcriptase (*see especially* col. 22, line 29-col. 24, line 45; *see also* col. 20, line 14-col. 22, line 9), whereby a nucleic acid molecule - with the inherent properties of reduced secondary structure and the reduced ability to cross-hybridize - is synthesized.

Appellant argues further that Vivekananda defines preferred nucleic acid aptamers as nucleic acids that bind to other molecules which do not encompass standard nucleic acid hydrogen bond formation exemplified by Watson-Crick base pair formation, but instead encompass all other types of non-covalent binding. Appellant is correct that Vivekananda teaches aptamers as a preferred embodiment. But, contrary to Appellant's assertions, the fact that aptamers are a preferred embodiment does not preclude Vivekananda as prior art of the instantly claimed invention because Vivekananda nevertheless teaches the synthesis of nucleic acids with the properties claimed, which properties are inherent in the nucleic acid molecules synthesized by Vivekananda. So, contrary to Appellant's assertions, these inherent properties existing in the nucleic acid molecules disclosed by Vivekananda do not change with the molecules' intended use.

Appellant also argues that Vivekananda does not teach an unstructured nucleic acid in which two complementary nucleotides of the unstructured nucleic acid do not form an intra-molecular base pair. This argument is unpersuasive in light of the teachings in columns 20-24, 29-31, where Vivekananda teaches the synthesis of nucleic acid ligands that contain modified nucleotides that render intra-strand,



complementary nucleotides with a reduced ability to form stable hydrogen bonded base pairs. The nucleic acids incorporating the modified nucleotides including, but not limited to, 2-amino deoxy purines, 2'-thio pyrimidines generate nucleic acid molecules with the inherent property of unstructured nucleic acids in which two complementary nucleotides of the unstructured nucleic acid (*i.e.* the nucleic acid strand that has incorporated within it the modified nucleic acid residues) do not form intramolecular base pairs, but hybridize with a complementary or second residue on a second strand.

Moreover, Vivekananda specifically discloses the incorporation of 2'-amino deoxy purines, 2'-thio substituted bases including 2'-thio cytidine and 2'-thio uridine, as well as the incorporation of inosine into nucleic acid ligands through various methods including PCR, RT-PCR, LCR, and several other nucleic acid amplification procedures. Vivekananda therefore teaches the instantly claimed methods of synthesizing nucleic acid polynucleotides with reduced secondary structure by incorporating the claimed modified bases, thereby producing nucleic acid strands with a reduced ability to form base pairs with complementary bases that are appropriately modified as claimed in the instant invention.

Claims 1 and 25-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Kutyaivin.

Appellant's arguments filed 2-8-06 have been fully considered but they are not persuasive. Appellant argues that Kutyaivin is not proper prior art because Kutyaivin teaches methods of producing polynucleotides with reduced ability to form inter-

molecular base pairs, as opposed to the instantly claimed invention, which teaches a method of producing polynucleotides with reduced ability to form intra-molecular base pairs.

Contrary to Appellant's assertions, Kutyavin teaches methods of synthesizing nucleic acid molecules with reduced secondary structure (see the abstract; col. 2, line 33- col. 9, line 53; claims 1-20, 23-25), comprising the polymerization of nucleotide precursors from a DNA or RNA template by an appropriate polymerase or transcriptase, (see col. 18 and 22-23), and which nucleotide precursors include 2-aminodeoxyadenosine 5'-triphosphate, 2-thiodeoxythymidine or -cytidine, 5'-triphosphate, pyrrolo-pyrimidine triphosphate, inosine triphosphate (see col. 5, col. 34, lines 53- 67), whereby a nucleic acid molecule with reduced levels of cross-hybridization is synthesized (see abstract; text in col. 4; claims 1-20) .

Appellant also argues that not all steps or features of the claimed invention are taught or suggested by Kuytavin because the instant claims have an embodiment that includes providing a nucleic acid template and providing nucleotides that have certain characteristics such that, when the nucleotides are polymerized to form an unstructured nucleic acid, the nucleotides do not form an intra-molecular base pair, as specified by the instant claims.

Contrary to Appellant's assertions, Kuyativin does disclose methods of synthesizing polynucleotides with a reduced ability to form self-annealing (e.g. intra-molecular) double strands by incorporating the modified bases claimed, which in turn render polynucleotides with reduced ability to form stable hydrogen bonded base pairs

with either a complementary strand or with complementary bases within the same strand (see e.g. col. 1 of Kutyaev et al: "[t]he ODNs include modified bases of such nature that the modified base forms stable hydrogen bonded base pairs with the natural partner base, but does not form stable hydrogen bonded base pairs with its modified partner... The ODNs of the invention, however, form substantially stable hybrids with the target sequence in each strand of duplex nucleic acid.").

See Table 1 and Table 2, cols. 23-24 of Kutyaev for specific examples of nucleic acid molecules generated by the instantly claimed methods, thereby generating modified base pairs incorporated into a single nucleic acid strand. The text in col. 23, lines 30-32 explains the existence of these pairs in a single strand: "The pair of SBC ODNs shown as Hybrid IV in Table 1 comprises two 28-mer sequences where each of the natural dG and dC nucleotides is replaced with dI and dP, respectively." And in col. 24, lines 25-26: "...SBC(V) and SBC(VI) are modified so that each dA and each dT is replaced with the d2amA and d2sT, respectively." So, contrary to Appellant's assertions, there is no distinction between the instantly claimed invention and the teachings of Kutyaev because both teach the incorporation of non-hydrogen bond-forming nucleotide pairs in the same nucleic acid molecule, which results in the decreased ability to form intra-molecular base pairs between complementary modified bases as instantly claimed.

The procedure disclosed by Kutyaev, therefore, is indistinguishable from the instantly claimed methods because they both involve the synthesis of oligonucleotides in the presence of modified bases to produce nucleic acid with reduced ability to

Art Unit: 1635

hybridize to complementary bases by reducing the ability to form Watson-Crick base pairing. This characteristic exists in intra-molecular as well as inter-molecular, complementary nucleic acid strands. Kuyativin properly anticipates the instantly claimed methods. The distinction between inter-molecular and intra-molecular base complementarity that is repeatedly stressed by Appellant to distinguish the instantly claimed invention from the prior art is also addressed by Kutyavin et al, albeit within the context of the target sequence: "It is known that secondary structure of mRNA and ribosomal RNA do not have two strands in the strict sense of that term. Nevertheless, unless the context otherwise indicates, in the present description the terminology "two strands" of double stranded nucleic acids also refers to the two complementary portions of duplex mRNA or of duplex ribosomal RNA as well. The general concept of double stranded DNA and of secondary structure ... is covered in this description by the term "duplex nuclei acid." (see col. 4).

For the above reasons, it is believed that the rejections should be sustained.

**(11) Related Proceeding(s) Appendix**

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

Respectfully submitted,

Application/Control Number: 09/358,141

Page 12

Art Unit: 1635

JZ

March 30, 2006

Conferees

Andrew Wang, SPE 1635

Remy Yucel, SPE 1636

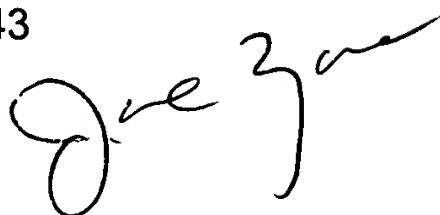
Agilent Technologies

Legal Department 51UPD

Intellectual Property Administration

PO Box 58043

Santa Clara, CA 95052-8043



**JANE ZARA, PH.D.  
PRIMARY EXAMINER**



**ANDREW WANG  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600**



**REMY YUCEL, PH.D  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600**